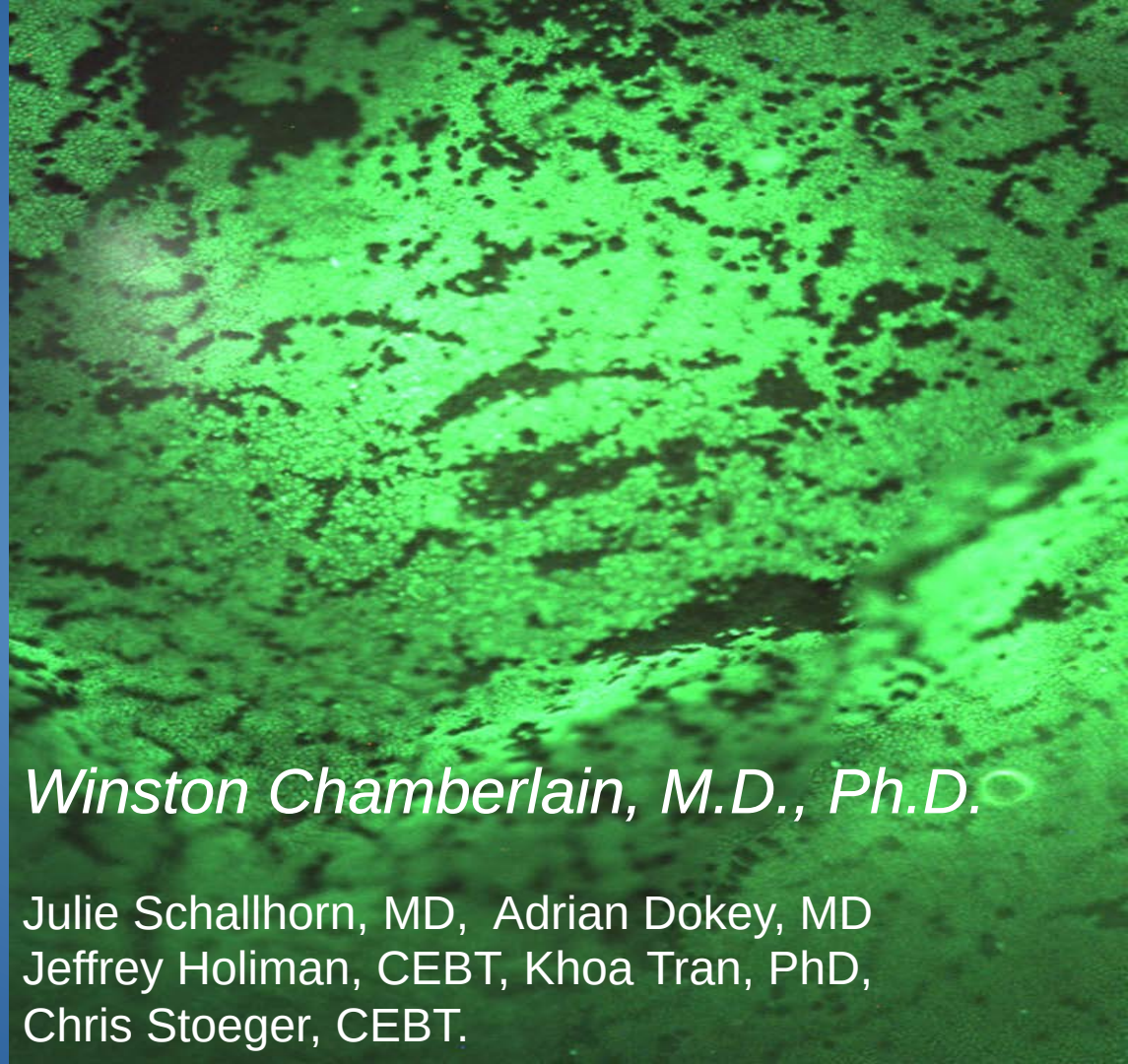
Plastic vs. Glass: DMEK Endothelial Cell Loss Due to Graft Injector Method

November 13, 2015



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CASEY EYE INSTITUTE
Oregon Health & Science University
OHSU

LIONS VISION GIFT

FINANCIAL DISCLOSURE

Nothing to disclose

Tissue Utilization Trends

Figure 2: Domestic DSEK Trends

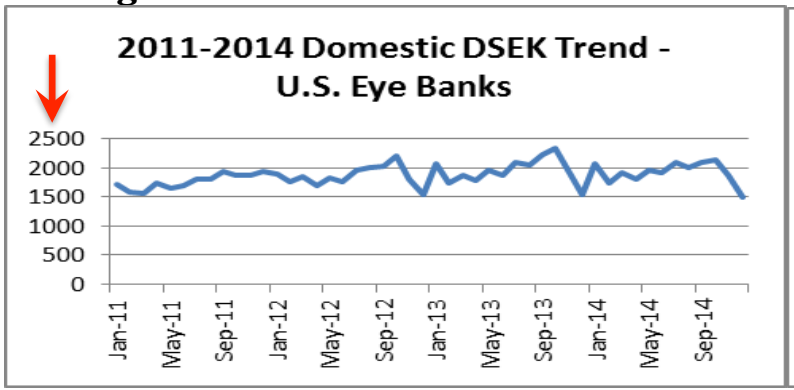


Figure 3: Domestic DMEK Trends

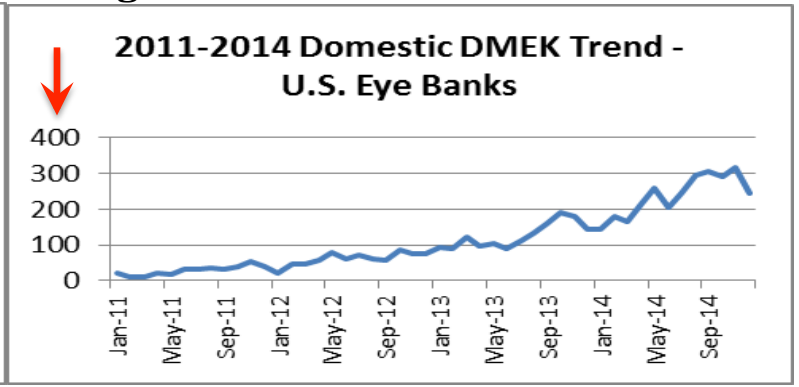
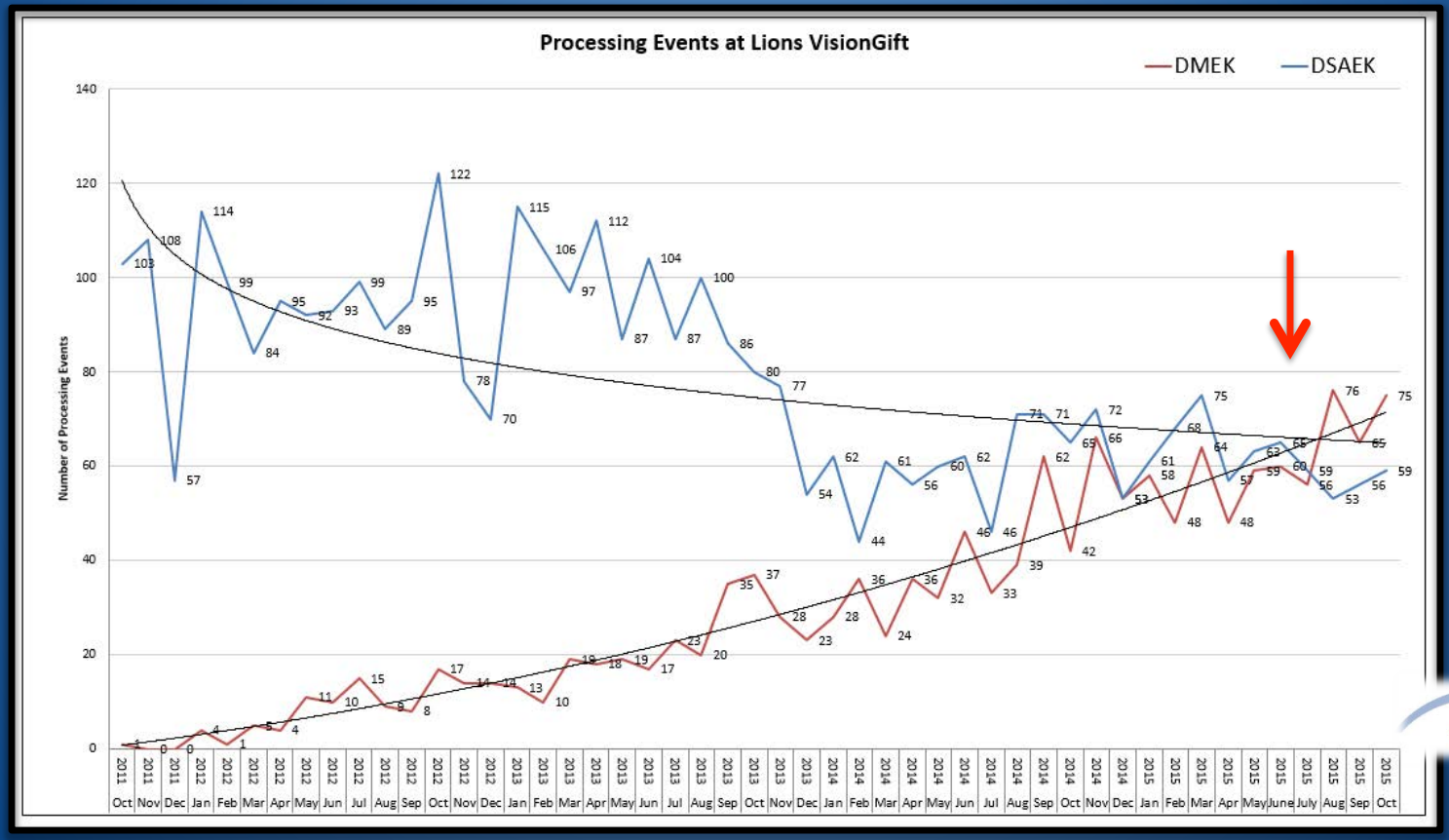


Table 4: Domestic Endothelial Keratoplasty Numbers Annual Comparison 2012 – 2014

Domestic Surgery Use	2014	2013	2012
Total Endothelial Keratoplasty Procedures	25,965	24,987	23,049
DSEK, DSAEK, DLEK Procedures	23,100	23,465	22,301
DMEK or DMAEK Procedures	2,865	1,522	748

Portland Eye Bank Utililization Trends Right Now

Lions VisionGift, Oregon



Background

- Variety of Surgical and Graft preparation techniques –*No Consensus*
  - Liarakos VS, Dapena I, Ham L, et al.. JAMA Ophthalmol 2013;131:29–35.
  - Yoeruek E, Bayyoud T, Hofmann J, et al. Cornea 2013;32:370–3.

- Variety of Insertion Methods—*No Consensus*

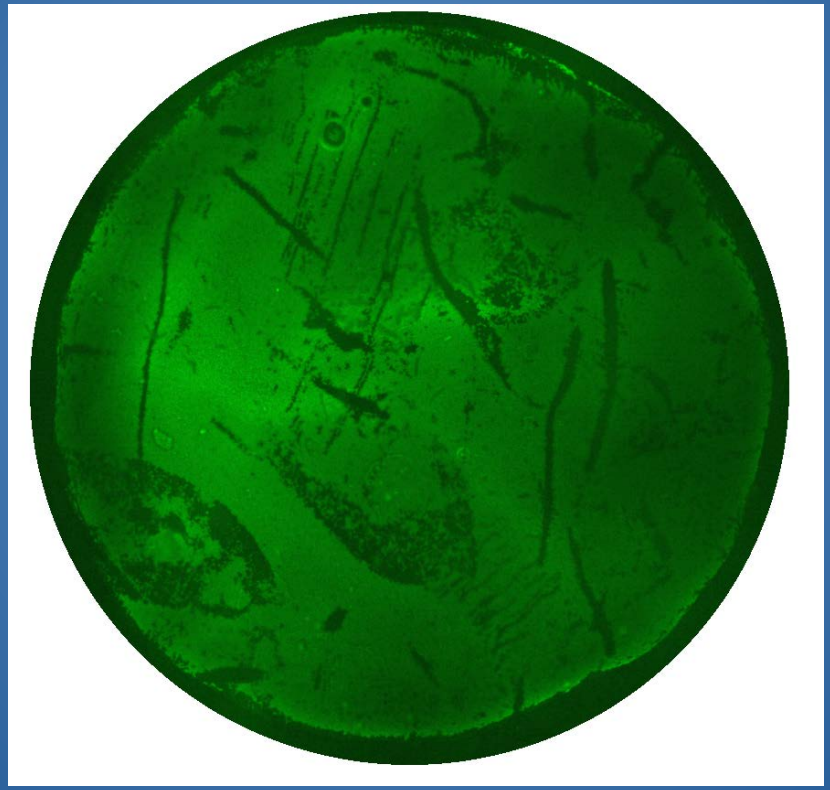
  Glass

  Dapena I, Moutsouris K, Droutsas K, et al. Arch Ophthalmol 2011; 129:88 – 94
  Yoeruek E, Bayyoud T, Hofmann J, Bartz-Schmidt KU.. Cornea 2013;32(3):370-3.
  Terry MA, Straiko MD, Veldman PB, et al. Cornea 2015.

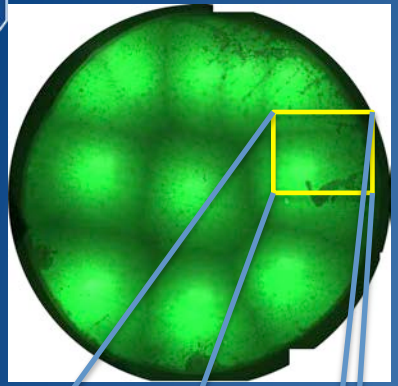
  Plastic
  - Modified IOL cartridges
    - Kruse FE, Laaser K, Cursiefen C, et al. Cornea 2011; 30:580 – 587.
    - Price MO, Price FW Jr. Curr Opin Ophthalmol 2013; 24:329–335.
    - Muraine M, Gueudry J, He Z, et al. Am J Ophthalmol 2013; 156:851 – 859.
    - Güell JL, Morral M, Gris O, et al. Cornea 2013; 32:1521 – 1526.
    - Kim EG, Todd L, Zhu A, Jun AS. Cornea. 2014 Jun;33(6):649-52.

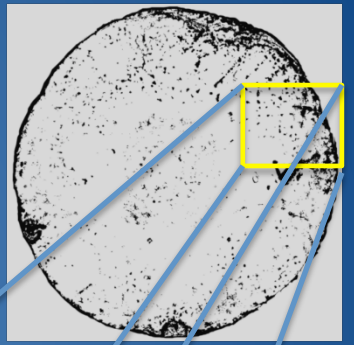
- Loading methods vary
  - Aspiration
  - “Pick up and put in” with forceps
- Dimensions of injectors differ greatly—
  - Radius of ejection orifice may not matter
    - Yoeruek E, Bartz-Schmidt KU, Hofmann J. Acta Ophthalmol. 2015 Jul 8.
- Ejection infusion pressures may differ significantly

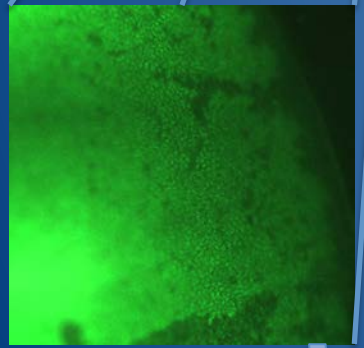
Patterns of Endothelial Cell Loss in DMEK tissues are Complex

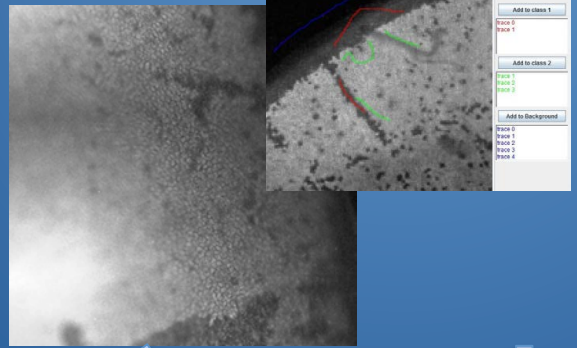


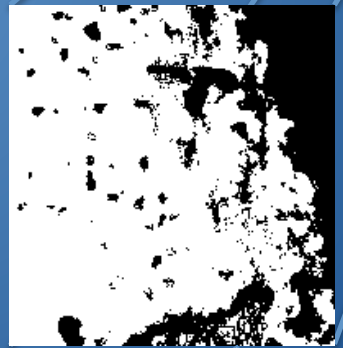
Segmentation To Find Cell Death Zones



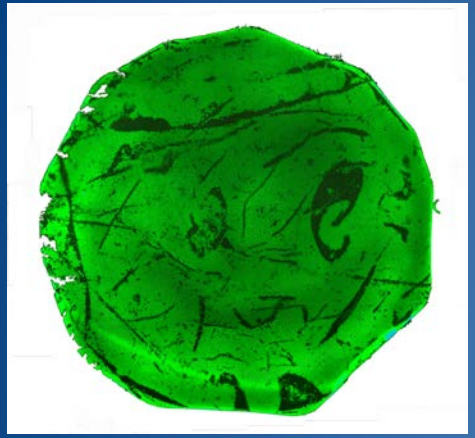


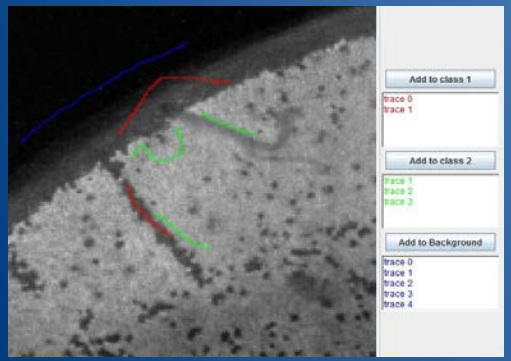






Complex Death Patterns and More Endothelial cell loss than anticipated





	%ECL as analyzed by Fiji				%ECL as analyzed by Adobe			
Sample	Reader 1	Reader 2	Reader 3	Average	Reader 1	Reader 2	Reader 3	Average
1	17.77	15.39	17.32	16.83	14.59	12.7	17.58	14.96
2	23.52	23.78	20.3	22.53	17.19	17.51	19.87	18.19
3	21.06	23.72	22.04	22.27	20.48	24.2	22.42	22.37
4	14.92	13.06	13.28	13.75	10.62	10.7	11.38	10.9
5	26.12	25.59	23.31	25.01	15.41	16.64	15.84	15.96
6	36.58	33.98	31.86	34.14	30.3	29.47	31	30.26
7	26.66	30.58	25.4	27.55	23.82	25.89	27.5	25.74
8	18.9	18.57	17.0	[illegible]	[illegible]0.58	11.89	10.2[illegible]	[illegible]
Average				22.5				18.66

Endothelial Cell Loss determined by 2 different methods

Jardine G, Holiman J, Stoeger C, Chamberlain WD
Curr Eye Res 2014

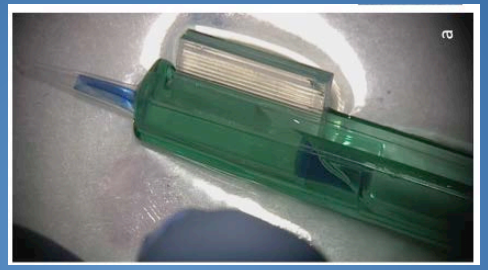
Graft Manipulation

Jones Tube--Glass

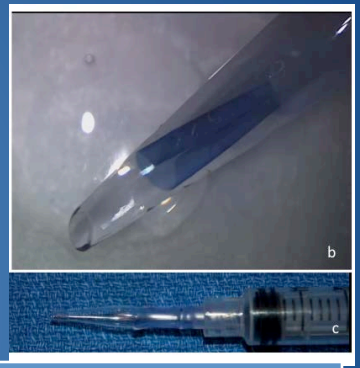
Viscoject (Endoject)--Plastic

Difference in Injector Parameters

Viscoject (Endoject)--Plastic



Jones Tube--Glass



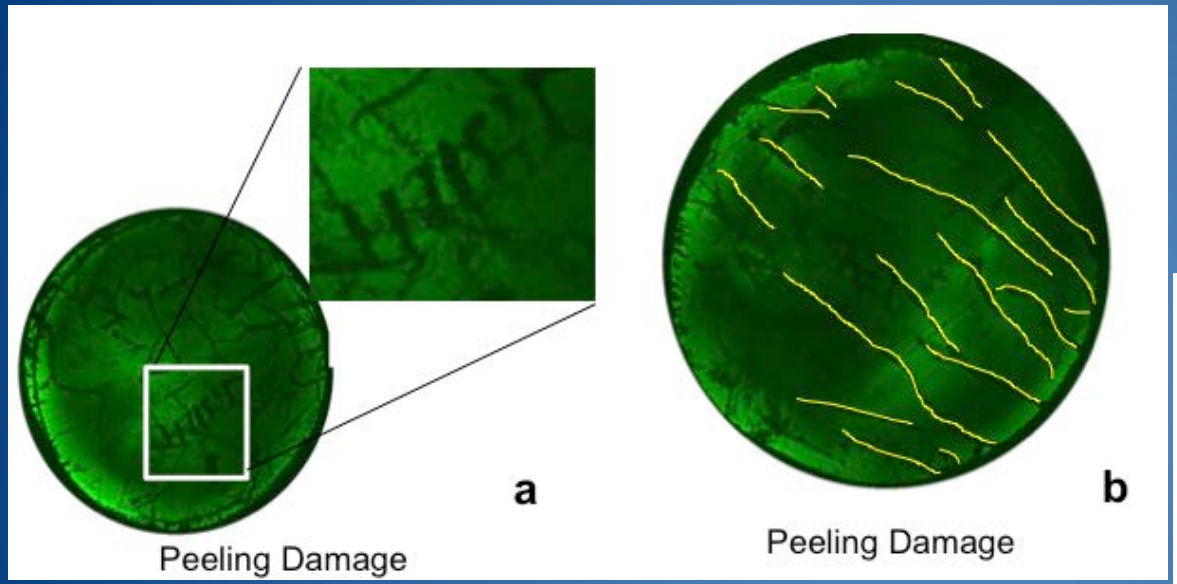
	Plastic	Glass
Average volume	0.13±0.004 cm^3	0.414±0.075 cm^3
Average Horizontal opening	1.91±0.04 mm	2.37±0.22 mm
Average Vertical opening	1.94±0.07 mm	2.40±0.05 mm
Average orifice area	2.91 mm^2	4.45 mm^2
	~150% larger area of opening	

Study Design

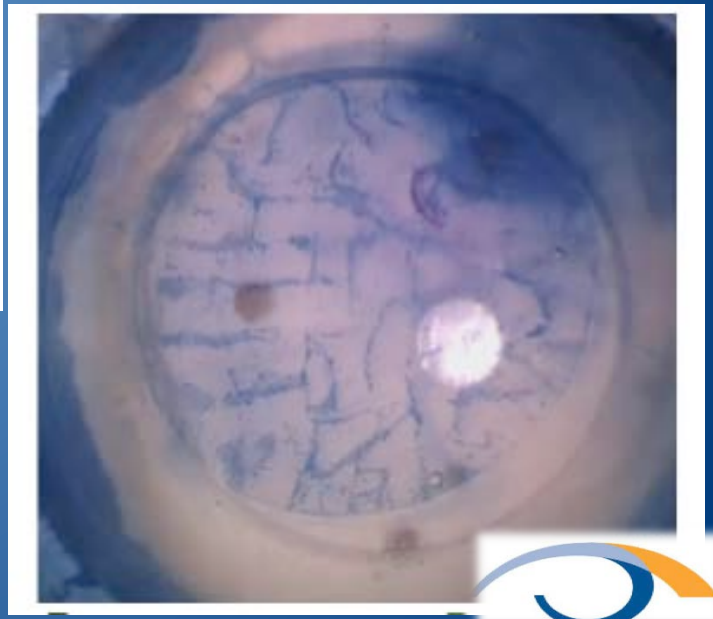
- Powered to detect a 10% difference in cell loss
- Confidence level of 90% (α= 0.05)
- 9 grafts for each injector 18 total (not suitable for transplantation)
- 2 Readers were masked to injector type
  - (no sig difference between 2 reader's results)

	Insertion Method		
	Modified Jones Tube	Viscoject	p-value
Donor Age (years)	61 ± 3	60 ± 3	0.2
range	50-74	52-73	
Death-to-Preservation (hours) range	11.4 ± 8	18.0 ± 10	0.1
	5-23	7-32	
Pre-Peel Cell Count	2484 ± 125	2717 ± 120	0.2
range	2012-3049	2045-3195	
Post-Peel Cell Count	2407 ± 127	2506 ± 153	0.6
range	1887-2941	1848-3247	

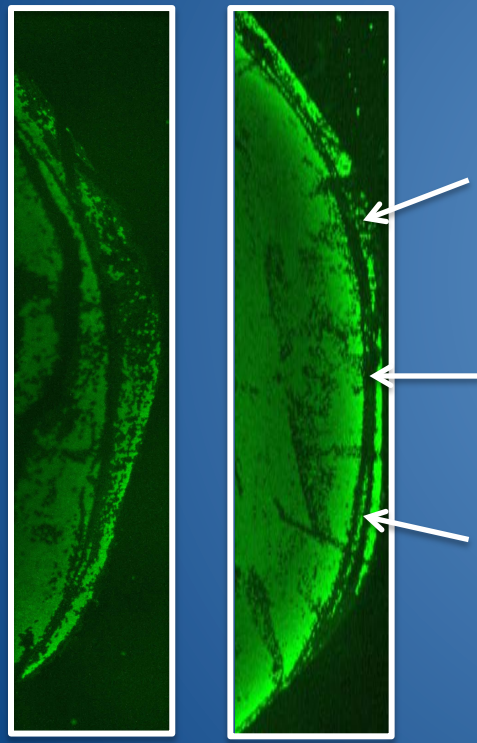
Peeling Damage Patterns



Heavy Damage after complete peel

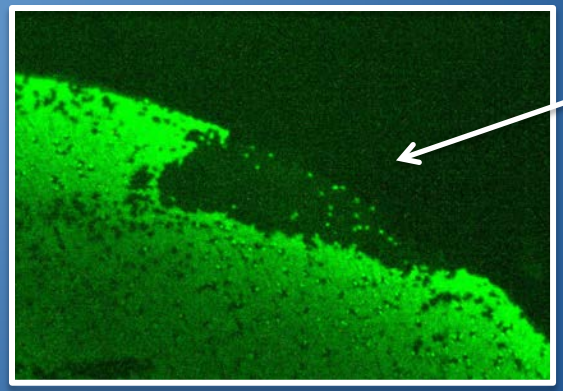


Trephination and Touch Damage

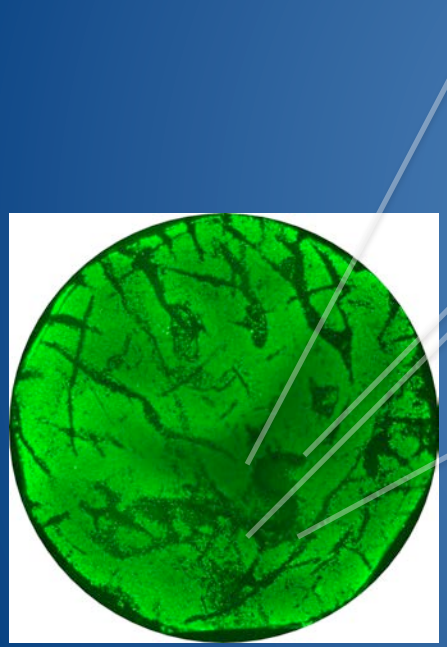


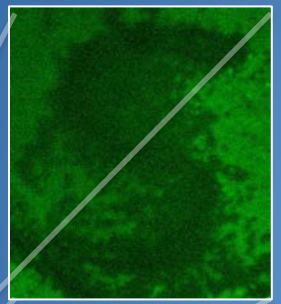
Trephination skipping

Forceps touch site

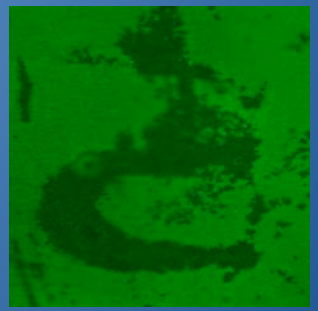


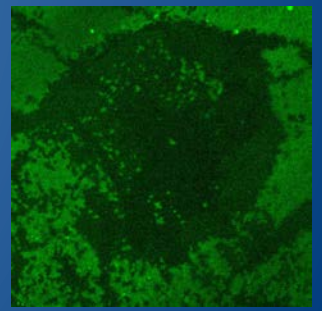
“S” Stamp Damage





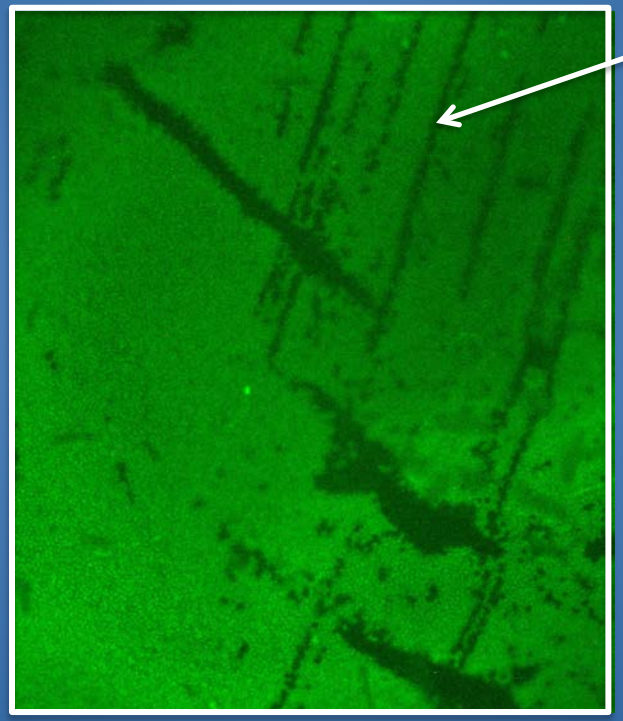
< 0.61% (±0.2%) cell death





Injector Damage

Viscoject 2.2



Modified Jones Tube

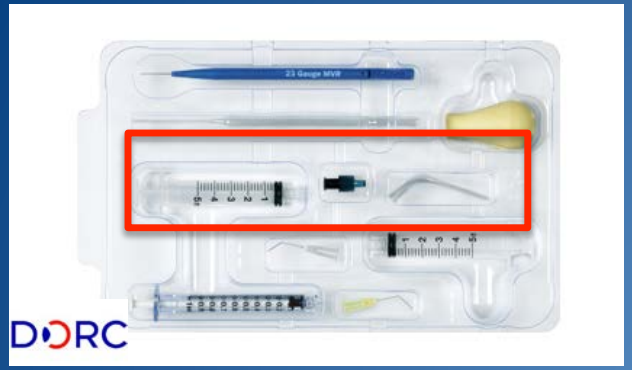
Fine Parallel “scrape” lines

NO sig difference between Glass and Plastic

We may be losing ~30% of cells by eye bank preparation and passage through tube into the eye

5-10% from injector step alone

	Insertion Method		
	Modified Jones Tube	Viscoject	p-value
Donor Age (years)	61 ± 3	60 ± 3	0.2
range	50-74	52-73	
Death-to-Preservation	11.4 ± 8	18.0 ± 10	0.1
(hours) range	5-23	7-32	
Pre-Peel Cell Count	2484 ± 125	2717 ± 120	0.2
range	2012-3049	2045-3195	
Post-Peel Cell Count	2407 ± 127	2506 ± 153	0.6
range	1887-2941	1848-3247	
%Cell Loss	27% ± 5%	32% ± 8%	0.3
95% confidence interval	24% to 29%	24% to 35%	
range	21% to 35%	21% to 47%	



- Recently commercially available in US
- No 510K approval
- Glass
- Requires smaller incision than other 2 injectors
- Potential advantages
  - smaller incision
  - Greater chamber stability
- Potential disadvantages
  - Cost
  - Damage to graft do to output radius of injector

DORC Glass injector

	Viscoject	Modified Jones Tube	DORC Glass Injector
Average volume	0.13±0.004 cm^3	0.414±0.075 cm^3	0.325±0.075 cm^3
Average Horizontal opening	1.91±0.04 mm	2.37±0.22 mm	IN: 3.82±0.01 mm OUT: 0.52±0.01 mm
Average Vertical opening	1.94±0.07 mm	2.40±0.05 mm	IN: 3.82±0.01 mm OUT: 0.685 ±0.01 mm
Average orifice area	2.91 mm^2	4.45 mm^2	IN: 11.4 mm^2 OUT:1.12 mm^2
Endothelial cell loss	32%±8%	27%±5%	30.6%±9%

Study weakness

- Powered to detect 10%, not less
- Tightness of scrolling could not be controlled (no age difference)
- Grafts were not actually injected into anterior chamber (possible difference in fluid dynamics)
- Grafts unfurled on a bed of viscoelastic

Conclusions

- No significant Difference in endothelial cell loss between Modified Jones tube (Glass) and Viscoject (Plastic) despite material and dimensional differences
- DORC Glass Injector may perform very similarly
- Parallel scrape marks visible regardless of injector type but reduced in DORC injector
- Near 30% ECD to peel and trephine graft and deliver it to anterior chamber (5-10% from the injector step alone)

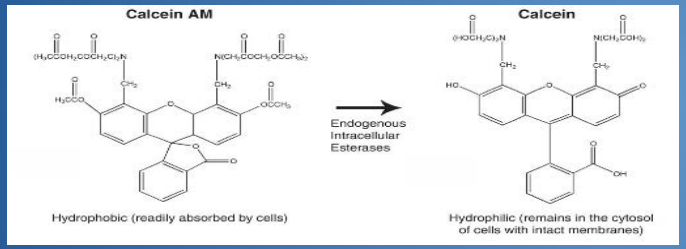
Acknowledgements

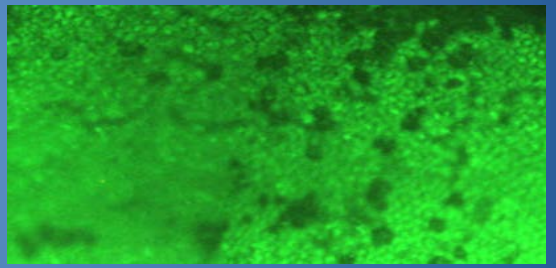
Julie Schallhorn, MD
Adrian Dokey, MD
Jeffrey Holiman, CEBT
Khoa Tran, PhD
Chris Stoeger CEBT

Lions VisionGift, Portland

Calcein AM Staining

- Cell permeable compound (Invitrogen, Inc.)
- It is hydrolyzed to strongly green fluorescent non-membrane permeable compound by esterases in live cells





- Retained in live cells with intact membrane
- More sensitive than Trypan blue methods due to functional and membrane integrity component of stain